UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/764,057	01/23/2004	Chin-Ming Chang	17273 CON1 CIP1 (AP)	7601

51957 7590 11/02/2006

ALLERGAN, INC.
2525 DUPONT DRIVE, T2-7H
IRVINE, CA 92612-1599

EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 11/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/764,057	CHANG ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) *38-45,52 and 53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-37,46-51 and 54* is/are rejected.

7)☒ Claim(s) *15 and 26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants Response to Restriction Requirement Acknowledged

1. Applicant's election, with traverse, with the Group I, claims 1-37, 46-51 and 54, is acknowledged. Applicants traverse the restriction requirement on the grounds that there would be no burden in searching the entire groups. This argument is not persuasive, as claimed invention would be distinctive, each from the other for the reason of the record. Furthermore, the search of the entire groups in the non-patent literature (a significant part of a thorough examination) would be burdensome. Therefore. The requirement is still deemed proper, and made Final. Claims 38-45 and 52-53 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected claims.

Drawings

2. Drawings submitted on January 23, 2004 are acceptable.

Priority

3. According to "Cross-Reference to Related Applications" in the specification, this application is a continuation-in-part of US Nonprovisional Application No.10/121,076, filed April 12, 2002, which is based upon U.S. Provisional Application No. 60/289,337 filed on May 7, 2001. Also, this application is a continuation-in-part of US Nonprovisional Application No.09/989,295, filed November 20, 2001, which is a continuation of U.S. Nonprovisional Application No. 09/388,968, filed on September 02, 1999, which is based upon U.S. Provisional Application No. 60/098,854, filed on September 02, 1998.

While the pharmaceutical composition comprising predisolone or prednisolone acetate, β-cyclodextrin, hydroxypropylmethylcellulose, preservative, buffer and NaCl (wherein said

pharmaceutical composition is prepared in ophthalmic solution, having pH in the range of about 5 to about 7 or about 4 or about 6 to about 9 or about 10 at least about 200 mOsmol/kg, more preferably in the range of about 200 to about 600 mOsmol/kg) was disclosed in the U.S. Provisional Application No. 60/289,337 and/or U.S. Provisional Application No. 60/098,854, the instantly claimed "a water-insoluble prodrug thereof", "hydroxypropyl-γ-cyclodextrin", the specific concentration of prednisolone acetate ("from 0.6% to 1.6%", "about 0.4%", "about 1.2%", "about 0.6%", "about 1.0%", "from 0.1% to 1.5%", or "greater than 0.5%"), hydroxypropyl-γ-cyclodextrin ("from about 10% to 25%", "about 25%" or "about 15%") and hydroxypropylmethylcellulose ("less than 1%", "from 0.05% to 0.4%" , "about 0.12%" or "from 0% to 0.15%"), "a chelating agent", "an osmolality of less than 300 mOsm/kg...", "the concentration of the cyclodextrin derivative is greater than 10%", "from 5% to 35% hydroxypropyl-β-cyclodextrin or hydroxypropyl-γ-cyclodextrin", and the specific pH of the solution ("a pH of from 4.5 to 5.5" or "about 4.8") were not disclosed in the priority documents. Therefore, the present invention directed to the subject matters were not disclosed in the priority documents (claims 1-3, 5-12, 17-23, 25-31, 33-37, 46 and 51) has an effective filing date of May 13, 2004.

Claim Objections

4. Claims 15 and 26 are objected to because of the following informalities: Misspelling of word "β-ydroxypropylmethylcellulose" (claim 15) and "hydroxpropylmethylcelluse" (claim 26) are present. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 13, 33-35, 46-50 and 54 rejected under 35 U.S.C. 102(b) as being anticipated by Lipari (US 4383992).

Lipari discloses a topical ophthalmic solution comprising 0.12% prednisolone such as prednisolone acetate, about 20% beta-cyclodextrin, about 0.5% hydroxypropylmethylcellulose that is useful for the treatment ocular inflammation (Example 1).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 2-12, 14-32, 36-37 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipari (US 4383992) in view of Loftsson (US 5472954), and further in view of Shinohara (5998488).

The teaching of Lipari has been discussed in above 35 USC 102(b) rejection.

Loftsson teaches a method of improving solubility and stability of pharmaceutical actives including prednisolone or prednisone by delivering the pharmaceutical actives in an aqueous solution comprising cyclodextrin (i.e., hydroxypropyl-β-cyclodextrin, hydroxypropyl-γ-cyclodextrin), water-soluble polymer (i.e., hydroxypropyl methylcellulose) and a lipophilic and/or water labile active ingredient (i.e., prednisolone and prednisone) and additives (i.e., buffers, preservatives, pH adjusting agents, chelating agent, etc...), wherein said solution is prepared in various dosage forms including ophthalmic formulation, preferably a sterile, isotonic, buffered aqueous solution (abstract; column 4, line thru column 5, line 50; column 6, line 29 thru column 7, line 43; column 9, line 38-39; column 13, line 65 thru column 14, line 25; column 19, lines 16-31; Example 11).

Shinohara is being supplied as reference to demonstrate the routine knowledge in using secondary agents such as chelating agent EDTA, cyclodextrins (e.g., β-cyclodextrin or γ-cyclodextrin) and NaCl in eye drops or ophthalmic solution.

The teaching of Lipari differs from the claimed invention in the use of cyclodextrin derivatives such as hydroxypropyl-β-cyclodextrin and hydroxypropyl-γ-cyclodextrin and excipients such as preservative, tonicifying agent, buffers and chelating agent. To incorporate such teaching into the teaching of Lipari, would have been obvious in view of Loftsson who teaches the use of cyclodextrin (i.e., hydroxypropyl-β-cyclodextrin, hydroxypropyl-γ-cyclodextrin) and water-soluble polymer (i.e., hydroxypropyl methylcellulose) in improving solubility and stability of steroid drug such as prednisolone and Shinohara who teaches the routine knowledge in using secondary agents such as EDTA and tonicifying agent such as NaCl in eye drops or ophthalmic solution.

It would have been obvious to one having ordinary skill in the art at the time of the invention was made to prepare the above taught composition in the effective amounts taught by applicant for with a reasonable expectation of success having above-cited references in combination. Thus, one would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

With respect to the specific pH range of the claimed composition, generally differences in an concentration or pH range will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such pH range are critical. Where the general conditions of a claim are disclosed in the prior art (especially ophthalmic preparation art), it is not inventive to discover the optimum or workable pH range by routine experimentation.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-37, 46-51 and 54 are rejected under the judicially created doctrine of double patenting over claims 5, 7-8 and 9-10 of U. S. Patent No. 6969706.

With respect to the claims 1, 4-13, 16-30, 32-35, 46-51 and 54,

Both the instant application and the patent are directed to a composition comprising prednisolone acetate, hydroxypropyl-γ-cyclodextrin, hydroxypropylmethylcellulose, preservative, chelating agent, buffer and tonicifying agent, wherein said composition has a pH of from 4.5 to 5.5.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly required the specific dosage amount of the active ingredient and inactive ingredients and NaCl as the tonicifying agent (see column 8, lines 4-5 of the USP'706) would have been obvious to a person of the ordinary skill in the art, especially in view of the dosage information provided in USP'706.

With respect to the claims 2-3, 14-15, 31, 36-37,

Reading the entire specification of USP'706 (including the claim 5 of USP'706), the skilled artisan would have known that substitution of hydroxypropyl-β-cyclodextrin for hydroxypropyl-γ-cyclodextrin would not alter the analogous properties of the composition due to close structural similarity of the compounds. One having ordinary skill in the art would have been motivated to make such modification to arrive at the claimed invention. Thus, USP'706 makes obvious the instant invention.

8. Claims 1-4, 13-15, 17-18, 46-51 and 54 are rejected under the judicially created doctrine of double patenting over claims 1-3 and 7-13 of U. S. Patent No. 6723353 or claims 1, 5 and 10-13 of U.S. Patent No. 6358935, and further in view of U. S. Patent No. 6969706.

The scope of the patented invention, which is drawn to a pharmaceutically acceptable composition comprising a liquid medium, a cyclodextrin component (the specification lists β-cyclodextrin and derivatives of β-cyclodextrin as a preferred cyclodextrin, see for example claim 3 of USP'353 and claim 5 of USP'935), a pharmaceutically active component (the specification lists prednisolone acetate as preferred therapeutic agent, see for example Examples 22-29 of USP'353and USP'935) and optionally with preservatives, overlaps with the scope of the instant invention.

Although the claims of USP'353 or USP'935 does not specifically recite the claimed water soluble polymer (i.e., hydroxypropylmethylcellulose), buffer, tonicifying agent and chelating agent in said composition, such determination of using known secondary agents involving each of the claimed formulation is routinely made by those of ordinary skill in the art

and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of the information provided in USP'706.

As discussed above, determination of appropriate dosage amount of the active ingredient and inactive ingredients involving each of the claimed formulation is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of the information provided in USP'706.

Conclusion

9. No Claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system,

see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon
Primary Patent Examiner
AU 1614

BRIAN-YONG S. KWON
PRIMARY EXAMINER